

CLAIMS

1. A method for detecting a mammalian cell proliferative disorder associated with a hypermutable target nucleic acid comprising isolating the nucleic acid present in a specimen of a mammal and detecting the presence of the hypermutable target nucleic acid.
2. The method of claim 1, wherein the hypermutable target nucleic acid is amplified before detecting.
3. The method of claim 2, wherein the amplification is by means of oligonucleotides which hybridize to the flanking regions of the hypermutable target nucleic acid.
4. The method of claim 1, wherein the target nucleic acid is selected from the group consisting of a nucleic acid deletion and a nucleic acid addition.
5. The method of claim 1, wherein the cell proliferative disorder is not due to a repair gene defect.
6. The method of claim 1, wherein the cell proliferative disorder is a neoplasm.
7. The method of claim 5, wherein the neoplasm is selected from the group consisting of the head, neck, lung, esophageal, stomach, small bowel, colon, bladder, kidney and cervix.
8. The method of claim 6, wherein the neoplasm is benign.

DETAILED DESCRIPTION

9. The method of claim 6, wherein the neoplasm is malignant.
10. The method of claim 1, wherein the specimen is selected from the group consisting of sputum, urine, bile, stool, cervical smears, saliva, tears, cerebral spinal fluid, regional lymph node and histopathologic margins.
11. The method of claim 1, wherein the target nucleic acid comprises the sequence $(X)_n$, wherein $X \neq 1$ nucleotide and wherein $n \geq 2$.
12. The method of claim 1, wherein the target nucleic acid comprises the sequence $(X)_n$, wherein $X \neq 2$ nucleotides and wherein $n \geq 2$.
13. The method of claim 12, wherein sequence X is selected from the group consisting of TC, AGC, TCC, CAG, CAA, CTG, AAAG, AGAT, and TCTT.
14. The method of claim 3, wherein the nucleotide sequence of the flanking region to which the oligonucleotide hybridizes is selected from the group of sequences consisting of:
- 5 a. 5'-CTT GTG TCC CGG CGT CTG-3' (SEQ ID NO:1);
 b. 5'-C AGC CCA GCA GGA CCA GTA-3' (SEQ ID NO:2);
 c. 5'-TGG TAA CAG TGG AAT ACT GAC-3' (SEQ ID NO:3);
 d. 5'-ACT GAT GCA AAA ATC CTC AAC-3' (SEQ ID NO:4);
 e. 5'-GA TGG GCA AAC TGC AGG CCT GGG AAG-3' (SEQ ID NO:5);
10 f. 5'-GCT ACA AGG ACC CTT CGA GCC CCG TTC-3' (SEQ ID NO:6);
 g. 5'-GAT GGT GAT GTG TTG AGA CTG GTG-3' (SEQ ID NO:7);
 h. 5'-GAG CAT TTC CCC ACC CAC TGG AGG-3' (SEQ ID NO:8);
 i. 5'-GTT CTG GAT CAC TTC GCG GA-3' (SEQ ID NO:9);
15 j. 5'-TGA GGA TGG TTC TCC CCA AG-3' (SEQ ID NO:10);

- RECEIVED
U.S. PATENT AND TRADEMARK OFFICE
JULY 10 1997
- 20
- k. 5'-AGT GGT GAA TTA GGG GTG TT-3' (SEQ ID NO:11);
 - l. 5'-CTG CCA TCT TGT GGA ATC AT-3' (SEQ ID NO:12);
 - m. 5'-CTG TGA GTT CAA AAC CTA TGG-3' (SEQ ID NO:13);
 - n. 5'-GTG TCA GAG GAT CTG AGA AG-3' (SEQ ID NO:14);
 - o. 5'-GCA CGC TCT GGA ACA GAT TCT GGA-3' (SEQ ID NO:15);
 - p. 5'-ATG AGG AAC AGC AAC CTT CAC AGC-3' (SEQ ID NO:16);
 - q. 5'-TCA CTC TTG TCG CCC AGA TT-3' (SEQ ID NO:17);
 - r. 5'-TAT AGC GGT AGG GGA GAT GT-3' (SEQ ID NO:18);
 - s. 5'-TGC AAG GAG AAA GAG AGA CTG A-3' (SEQ ID NO:19);
 - t. 5'-AAC AGG ACC ACA GGC TCC TA-3' (SEQ ID NO:20); and
 - u. sequences complementary to sequences a. through t.
- 25
15. The method of claim 14 wherein the oligonucleotide is selected from the group consisting of:
- a. 5'-CAG ACG CCG GGA CAC AAG-3' (SEQ ID NO:21);
 - b. 5'-TAC TGG TCG TGC TGG GCT G-3' (SEQ ID NO:22);
 - c. 5'-GTC AGT ATT ACC CTG TTA CCA-3' (SEQ ID NO:23);
 - d. 5'-GTT GAG GAT TTT TGC ATC AGT-3' (SEQ ID NO:24);
 - e. 5'-CTT CCC AGG CCT GCA GTT TGC CCA TC-3'(SEQ ID NO:25);
 - f. 5'-GAA CGG GGC TCG AAG GGT CCT TGT AGC-3' (SEQ ID NO:26);
 - 10 g. 5'-CAC CAG TCT CAA CAC ATC ACC ATC-3'(SEQ ID NO:27);
 - h. 5'-CCT CCA GTG GGT GGG GAA ATG CTC-3' (SEQ ID NO:28);
 - i. 5'-TCC GCG AAG TGA TCC AGA AC-3'(SEQ ID NO:29);
 - j. 5'-CTT GGG GAG AAC CAT CCT CA-3'(SEQ ID NO:30);
 - 15 k. 5'-AAC ACC CCT AAT TCA CCA CT-3'(SEQ ID NO:31);
 - l. 5'-ATG ATT CCA CAA GAT GGC AG-3'(SEQ ID NO:32);
 - m. 5'-CCA TAG GTT TTG AAC TCA CAG-3'(SEQ ID NO:33);
 - n. 5'-CTT CTC AGA TCC TCT GAC AC-3'(SEQ ID NO:34);

- o. 5'-TCC AGA ATC TGT TCC AGA GCG TGC-3'(SEQ ID NO:35);
20 p. 5'-GCT GTG AAG GTT GCT GTT CCT CAT-3'(SEQ ID NO:36);
q. 5'-AAT CTG GGC GAC AAG AGT GA-3'(SEQ ID NO:37);
r. 5'-ACA TCT CCC CTA CCG CTA TA-3'(SEQ ID NO:38);
s. 5'-TCA GTC TCT CTT TCT CCT TGC A-3' (SEQ ID NO:39);
t. 5'-TAG GAG CCT GTG GTC CTG TT-3' (SEQ ID NO:40); and
25 u. sequences complementary to sequences a. through t.
16. The method of claim 1, wherein the hypermutable target nucleic acid is selected from the group of microsatellite loci consisting of ARA, D14S50, AR, MD, SAT, DRPLA, ACTBP2, FGA, D4S243 and UT762.
17. A kit useful for the detection of a mammalian cell proliferative disorder associated with a ~~hypermutable target~~ nucleic acid from a tissue specimen, the kit comprising carrier means being compartmentalized to receive in close confinement therein one or more containers containing oligonucleotide primers which hybridize to flanking nucleic acid sequences of a hypermutable target nucleic acid.
5
18. The kit of claim 17, wherein the specimen is selected from the group consisting of sputum, urine, bile, stool, cervical smears, saliva tears, cerebral spinal fluid, regional lymph node and histopathologic margins.
19. The kit of claim 17, wherein the kit further comprises a detectably labeled deoxynucleotide.
20. The kit of claim 17, wherein the target nucleic acid is a microsatellite DNA locus.

21. The kit of claim 20, wherein the microsatellite locus is selected from the group of loci consisting of ARA, D14S50, AR, MD, SAT, DRPLA, ACTBP2, FGA, and UT762.
22. The kit of claim 21, wherein the loci are multiplexed.

ADD B1

ADD E3

ADD J27

PRINTED IN U.S.A. 100% RECYCLED